In re Appln. of Burke, Jr., et al.
Application No. 09/937,150

CLAIM AMENDMENTS

Claims 1-38. (Canceled)

39. (Currently Amended) A compound of the formula:

$$W\text{-}Y\text{-}(AA)_n\text{-}Z$$

wherein n is 1 to 15;

Y is a phenylalanyl radical having a phenyl ring, an amine end, ~~and~~ a carboxyl end, and a -$CH_2CH<$ group attached to the phenyl ring at the -CH_2 and the amine end and the carboxyl end attached to the CH<, the phenyl ring having one or more substituents selected from the group consisting of hydroxyl, carboxyl, formyl, carboxyalkyl, carboxyalkyloxy, dicarboxyalkyl, dicarboxyalkyloxy, dicarboxyhaloalkyl, dicarboxyhaloalkyloxy, and phosphonoalkyl, phosphonohaloalkyl, wherein the alkyl portion of the substituents of the phenyl ring may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, aminoalkyl, alkyl, and alkoxy~~, and keto~~;

W is a moiety attached to the nitrogen of Y and is selected from the group consisting of alkylcarbonyl, oxalyl, alkylaminooxalyl, arylaminooxalyl, arylalkylaminooxalyl, alkoxyoxalyl, carboxyalkyl carbonyl, heterocyclyl carbonyl, heterocyclylalkyl carbonyl, arylalkyl heterocyclylalkyl carbonyl, aryloxycarbonyl, and arylalkoxycarbonyl, wherein the aryl and alkyl portions of ~~the substituents~~ W may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, ~~carboxyl, amino~~, aminoalkyl, alkyl, and alkoxy; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S;

AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

Z is arylalkylamino or aryl heterocyclyl C_1-C_6 alkylamino wherein an aryl group, which may be substituted or unsubstituted, is linked to a heterocyclyl group; wherein aryl is a carbocyclic aryl;

or a salt thereof;

with the proviso that Z is not arylalkylamino when W is oxalyl or acetyl and the phenyl ring of phenylalanyl contains a hydroxyl, malonyl difluoromethyl, malonyloxy, carboxyalkyloxy, phosphonodifluoromethyl, or phosphonomethyl substituent on the phenyl ring at a position para to the ~~CH_2 CH group~~ $-CH_2CH<$ group ~~of phenylalanyl~~ and the ortho and meta positions are unsubstituted and the proviso that Z is not arylalkylamino when W is arylalkoxycarbonyl and the susbstituent on the phenyl ring of Y is phosphonomethyl.

40. (Currently Amended) A compound of the formula: $W\text{-}Y\text{-}(AA)_n\text{-}Z$ wherein n is 1 to 15;

Y is a phenylalanyl radical having a phenyl ring, an amine end, ~~and~~ a carboxyl end, and a $-CH_2CH<$ group attached to the phenyl ring at the $-CH_2$ and the amine end and the carboxyl end attached to the $CH<$, the phenyl ring having one or more substituents selected from the group consisting of hydroxyl, carboxyl, formyl, carboxy C_1-C_6 alkyl, carboxy C_1-C_6 alkyloxy, dicarboxy C_1-C_6 alkyl, dicarboxy C_1-C_6 alkyloxy, dicarboxyhalo C_1-C_6 alkyl, dicarboxyhalo C_1-C_6 alkyloxy, and phosphono C_1-C_6 alkyl, phosphonohalo C_1-C_6 alkyl, wherein the alkyl portion of the substituents of the phenyl ring may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, aminoalkyl, C_1-C_6 alkyl, and C_1-C_6 alkoxy~~, and keto~~;

W is a moiety attached to the nitrogen of Y and is selected from the group consisting of C_1-C_6 alkylcarbonyl, oxalyl, C_1-C_6 alkylaminooxalyl, arylaminooxalyl, aryl C_1-C_6 alkylaminooxalyl, C_1-C_6 alkoxyoxalyl, carboxy C_1-C_6 alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C_1-C_6 alkyl carbonyl, aryl C_1-C_6 alkyl heterocyclyl C_1-C_6 alkyl carbonyl, aryloxycarbonyl, and aryl C_1-C_6 alkoxycarbonyl, wherein the aryl and alkyl portions of ~~the substituents~~ W may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, ~~carboxyl, amino,~~ amino C_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 alkoxy; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S;

AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

Z is aryl C_1-C_6 alkylamino or arylheterocyclyl C_1-C_6 alkylamino wherein an aryl group is linked to a heterocyclyl group; wherein aryl is a carbocyclic aryl group;

or a salt thereof;

with the proviso that Z is not aryl C_1-C_6 alkylamino when W is oxalyl or acetyl and the phenyl ring of phenylalanyl contains a hydroxyl, dicarboxyhaloalkyl, dicarboxyalkoxy, carboxyalkyloxy, phosphonoalkyl, or phosphonohaloalkyl substituent of the phenyl ring at a position para to the ~~CH_2-CH- group~~ $-CH_2CH<$ group ~~of phenylalanyl~~ and the ortho and meta positions are unsubstituted and the proviso that Z is not arylalkylamino when W is aryl methoxycarbonyl when the susbstituent on the phenyl ring of Y is phosphonomethyl.

41. (Currently Amended) A compound of the formula:

W-Y-$(AA)_n$-Z wherein n is 1 to 15;

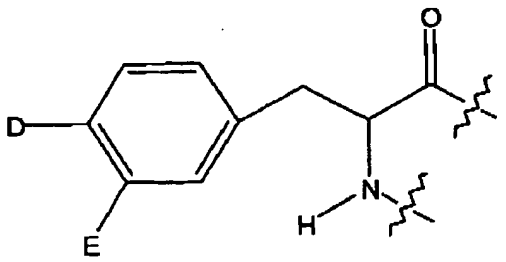
W is a moiety attached to the nitrogen of Y and is selected from the group consisting of C_1-C_6 alkylcarbonyl, oxalyl, C_1-C_6 alkylaminooxalyl, arylaminooxalyl, aryl C_1-C_6 alkylaminooxalyl, C_1-C_6 alkoxyoxalyl, carboxy C_1-C_6 alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C_1-C_6 alkyl carbonyl, aryl C_1-C_6 alkyl heterocyclyl C_1-C_6 alkyl carbonyl, aryloxycarbonyl, and aryl C_1-C_6 alkoxycarbonyl, wherein the aryl and alkyl portions of W may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 alkoxy; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S;

AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

Z is aryl C_1-C_6 alkylamino or arylheterocyclyl C_1-C_6 alkylamino wherein an aryl group is linked to a heterocyclyl group; wherein aryl is a carbocyclic aryl group;

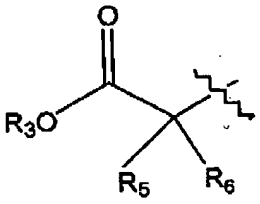
or a salt thereof;

~~The compound of claim 40,~~ wherein Y is of the formula XI:

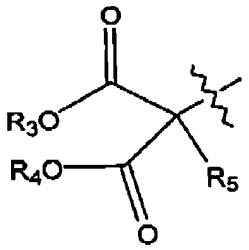


(XI)

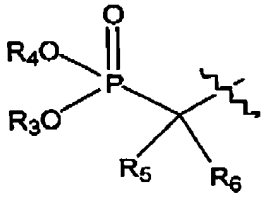
wherein D has the formula XII, XIII, or XIV:



(XII)



(XIII)



(XIV)

wherein R_3 and R_4 may be the same or different and are selected from the group consisting of hydrogen, C_1-C_6 alkyl, aryl, aryl C_1-C_6 alkyl, C_1-C_6 alkaryl, and heteroaryl; and R_5 and R_6 may be the same or different and are selected from the group consisting of hydrogen, halo, hydroxy, amino, and C_1-C_6 alkoxy; and

E is selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylcarbonyl, carboxyl, and C_1-C_6 alkylcarbonyl C_1-C_6 alkyl;

with the proviso that Z is not aryl C_1-C_6 alkylamino when W is oxalyl or acetyl and D is hydroxyl, dicarboxyhaloalkyl, dicarboxyalkoxy, carboxyalkyloxy, alkoxycarbonylalkyl, phosphonoalkyl, or phosphonohaloalkyl and E is hydrogen.

42. (Previously Presented) The compound of claim 41, wherein D is of formula XII.

43. (Previously Presented) The compound of claim 41, wherein D is of formula XIII.

44. (Previously Presented) The compound of claim 41, wherein D is of formula XIV.

45. (Previously Presented) The compound of claim 42, wherein E is hydrogen.

46. (Previously Presented) The compound of claim 42, wherein E is carboxyl.

47. (Currently Amended) The compound of claim 42, wherein R_3, ~~R_4~~, R_5, and R_6 are hydrogen.

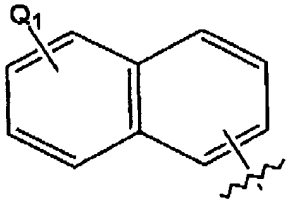
48. (Previously Presented) The compound of claim 44, wherein R_3 and R_4 are hydrogen.

49. (Currently Amended) The compound of claim 39, wherein W is selected from the group consisting of C_1-C_6 alkylcarbonyl, oxalyl, C_1-C_6 alkylaminooxalyl, arylaminooxalyl, aryl C_1-C_6 alkylaminooxalyl, C_1-C_6 alkoxyoxalyl, carboxy C_1-C_6 alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C_1-C_6 alkyl carbonyl, aryl C_1-C_6 alkyl heterocyclyl C_1-C_6 alkyl carbonyl, aryloxycarbonyl, and aryl C_1-C_6 alkoxycarbonyl, wherein the aryl and alkyl portions of ~~the substituents~~ W may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 alkoxy; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S.

50-66. (Canceled)

67. (Previously Presented) The compound of claim 40, wherein Z is aryl C_1-C_6 alkylamino.

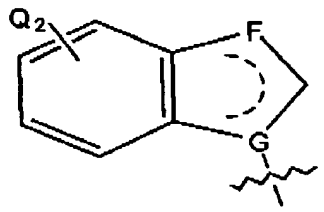
68. (Previously Presented) The compound of claim 67, wherein the aryl portion of Z has the formula:



wherein Q_1 is hydrogen or a substituent selected from the group consisting of hydroxyl, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, amino, and C_1-C_6 acylamino.

69-72. (Canceled)

73. (Currently Amended) The compound of claim 39, wherein the aryl heterocyclyl portion of Z has the formula:



wherein Q_2 is hydrogen or a substituent selected from the group consisting of hydroxyl, halo, C_1-C_6 alkyl, C_1-C_6 alkoxy, amino, and C_1-C_6 acylamino, and F and G are independently selected from the group consisting of C, N, O, and S; with the proviso that F and G are not simultaneously C.

74-77. (Canceled)

78. (Previously Presented) The compound of claim 39, wherein said amino acid is selected from the group consisting of glycine, alanine, valine, norvaline, leucine, iso-leucine, norleucine, α-amino n-decanoic acid, serine, homoserine, threonine, methionine, cysteine, S-acetylaminomethyl-cysteine, proline, trans-3- and trans-4-hydroxyproline, phenylalanine, tyrosine, 4-aminophenylalanine, 4- nitrophenylalanine, 4-chlorophenylalanine, 4-carboxyphenylalanine, β-phenylserine β-hydroxyphenylalanine, phenylglycine, α-naphthylalanine, cyclohexylalanine, cyclohexylglycine, tryptophan, indoline-2-carboxylic acid, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, aspartic acid, asparagine, aminomalonic acid, aminomalonic acid monoamide, glutamic acid, glutamine, histidine, arginine, lysine, N'-benzyl-N'-methyl-lysine, N',N'-dibenzyl-lysine, 6-hydroxylysine, ornithine, α-aminocyclopentane carboxylic acid, α-aminocyclohexane carboxylic acid, α-aminocycloheptane carboxylic acid, α-(2-amino-2-norbornane)-carboxylic acid, α,γ-diaminobutyric acid, α,β-diaminopropionic acid, homophenylalanine, and α-tert-butylglycine.

79-84. (Canceled)

85. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 39.

86-115. (Canceled)

116. (Currently Amended) A compound of the formula:

$$W\text{-}Y\text{-}(AA)_n\text{-}Z$$

wherein n is 0 to 15;

Y is a phenylalanyl radical having a phenyl ring, an amine end, and a carboxyl end, a $\text{-}CH_2CH<$ group attached to the phenyl ring at the CH_2 and the amine end and the carboxyl end are attached to the CH<, the phenyl ring having the following substituent or a combination of substituents: (i) dicarboxy C_1-C_6 alkyl, (ii) hydroxyl and carboxy C_1-C_6 alkyl, (iii) carboxyl and carboxy C_1-C_6 alkyl, or (iv) ~~dicarboxyhalo C_1-C_6 alkyl, or~~ dicarboxyhalo C_1-C_6 alkyloxy; or an ester of (i), (ii), (iii), or (iv); wherein the alkyl portion of the substituents of the phenyl ring may be unsubstituted or substituted with a substituent selected from the group consisting of ~~halo,~~ hydroxy, carboxyl, amino, aminoalkyl, C_1-C_6 alkyl, and C_1-C_6 alkoxy~~, and keto~~;

W is a moiety attached to the nitrogen of Y and is selected from the group consisting of C_1-C_6 alkylcarbonyl, oxalyl, C_1-C_6 alkylaminooxalyl, arylaminooxalyl, aryl C_1-C_6 alkylaminooxalyl, C_1-C_6 alkoxyoxalyl, carboxy C_1-C_6 alkyl carbonyl, heterocyclyl carbonyl, heterocyclyl C_1-C_6 alkyl carbonyl, aryl C_1-C_6 alkyl heterocyclyl C_1-C_6 alkyl carbonyl, aryloxycarbonyl, and aryl C_1-C_6 alkoxycarbonyl, wherein the aryl and alkyl portions of ~~the substituents~~ W may be unsubstituted or substituted with a substituent selected from the group consisting of halo, hydroxy, carboxyl, amino, amino C_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 alkoxy; and the heterocyclyl portion of W contains at least 4 hetero atoms selected from the group consisting of O, N, and S;

AA is an amino acid, the amine end of which is attached to the carboxyl end of Y; and

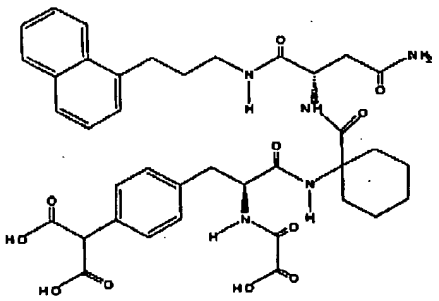
Z is aryl C_1-C_6 alkylamino or arylheterocyclyl C_1-C_6 alkylamino wherein an aryl group is linked to a heterocyclyl group; wherein aryl is a carbocyclic aryl;

or a salt thereof.

117. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 116.

118-119. (Canceled)

120. (Currently Amended) The compound of claim 39, which is of the formula:



121. (Currently Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound of claim 120.

122. (Previously Presented) A method for inhibiting an SH2 domain of a protein from binding with a phosphoprotein comprising contacting the SH2 domain with the compound of claim 120.

123. (Currently Amended) A method of ~~preventing or treating a disease, state, or condition, in a mammal comprising administering~~ inhibiting proliferation of cells in a patient that exhibit erb-2 signalling comprising contacting the cells with the compound of claim 120.

124. (Currently Amended) A method of inhibiting MAP kinase activity in a mammal comprising administering to the mammal in need thereof the compound of claim 120.

125. (Canceled)

126. (Previously Presented) The compound of claim 116, wherein n is 1-3.

127. (Previously Presented) The compound of claim 116, wherein Z is naphthylpropylamino.

128. (Previously Presented) The compound of claim 116, wherein the phenyl ring of Y includes a malonyl group.

129. (Previously Presented) The compound of claim 116, wherein the phenyl ring of Y includes a carboxymethyl group and a hydroxyl group.

130. (Previously Presented) The compound of claim 116, wherein said amino acid is selected from the group consisting of glycine, alanine, leucine, isoleucine, norleucine, cyclohexylalanine, 4-aminocyclohexylglycine, 4-acetylaminocyclohexylglycine, aspartic acid, asparagine, glutamic acid, and glutamine.

131-132. (Canceled)

133. (Currently Amended) A method for treating breast cancer in a patient comprising administering to the patient an effective amount of the compound of claim 120.

134-135. (Canceled)

136. (Currently Amended) A method of enhancing the therapeutic effect of a cancer treatment rendered to a mammal that has been afflicted with a cancer, comprising administering to the mammal the compound of claim 120 in conjunction with the treatment, wherein the treatment comprises chemotherapy, radiation therapy, or biological therapy.

137-139. (Canceled)

140. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 40.

141. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 41.

142. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 42.

143. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 43.

144. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 44.

145. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 49.

146. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 68.

147. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 73.

148. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of claim 78.

149. (New) A method for inhibiting an SH2 domain of a protein from binding with a phosphoprotein comprising contacting the SH2 domain with the compound of claim 39.

150. (New) A method for inhibiting an SH2 domain of a protein from binding with a phosphoprotein comprising contacting the SH2 domain with the compound of claim 40.

151. (New) A method for inhibiting an SH2 domain of a protein from binding with a phosphoprotein comprising contacting the SH2 domain with the compound of claim 41.

152. (New) A method of inhibiting proliferation of cells in a patient that exhibit erb-2 signaling comprising contacting the cells with a compound of claim 39.

153. (New) A method of inhibiting proliferation of cells in a patient that exhibit erb-2 signaling comprising contacting the cells with a compound of claim 40.

154. (New) A method of inhibiting proliferation of cells in a patient that exhibit erb-2 signaling comprising contacting the cells with a compound of claim 41.

155. (New) A method for inhibiting the growth of human breast cancer cells comprising contacting the cells with a compound of claim 39.

156. (New) A method for inhibiting the growth of human breast cancer cells comprising contacting the cells with a compound of claim 40.

157. (New) A method for inhibiting the growth of human breast cancer cells comprising contacting the cells with a compound of claim 41.

158. (New) A method for inhibiting the growth of human breast cancer cells comprising contacting the cells with a compound of claim 116.